

§514.116 Notice of withdrawal of approval of application.

When an approval of an application submitted pursuant to section 512 of the act is withdrawn by the Commissioner, he will give appropriate public notice of such action by publication in the FEDERAL REGISTER.

§514.117 Adequate and well-controlled studies.

(a) *Purpose.* The primary purpose of conducting adequate and well-controlled studies of a new animal drug is to distinguish the effect of the new animal drug from other influences, such as spontaneous change in the course of the disease, normal animal production performance, or biased observation. One or more adequate and well-controlled studies are required to establish, by substantial evidence, that a new animal drug is effective. The characteristics described in paragraph (b) of this section have been developed over a period of years and are generally recognized as the essentials of an adequate and well-controlled study. Well controlled, as used in the phrase adequate and well controlled, emphasizes an important aspect of adequacy. The Food and Drug Administration (FDA) considers these characteristics in determining whether a study is adequate and well controlled for purposes of section 512 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360b). Adequate and well-controlled studies, in addition to providing a basis for determining whether a new animal drug is effective, may also be relied upon to support target animal safety. The report of an adequate and well-controlled study should provide sufficient details of study design, conduct, and analysis to allow critical evaluation and a determination of whether the characteristics of an adequate and well-controlled study are present.

(b) *Characteristics.* An adequate and well-controlled study has the following characteristics:

(1) The protocol for the study (protocol) and the report of the study results (study report) must include a clear statement of the study objective(s).

(2) The study is conducted in accordance with an appropriate standard of

conduct that addresses, among other issues, study conduct, study personnel, study facilities, and study documentation. The protocol contains a statement acknowledging the applicability of, and intention to follow, a standard of conduct acceptable to FDA. The study report contains a statement describing adherence to the standard.

(3) The study is conducted with a new animal drug that is produced in accordance with appropriate manufacturing practices, which include, but are not necessarily limited to, the manufacture, processing, packaging, holding, and labeling of the new animal drug such that the critical characteristics of identity, strength, quality, purity, and physical form of the new animal drug are known, recorded, and reproducible, to permit meaningful evaluations of and comparisons with other studies conducted with the new animal drug. The physical form of a new animal drug includes the formulation and physical characterization (including delivery systems thereof, if any) of the new animal drug as presented to the animal. The protocol and study report must include an identification number which can be correlated with the specific formulation and production process used to manufacture the new animal drug used in the study.

(4) The study uses a design that permits a valid comparison with one or more controls to provide a quantitative evaluation of drug effects. The protocol and the study report must describe the precise nature of the study design, e.g., duration of treatment periods, whether treatments are parallel, sequential, or crossover, and the determination of sample size. Within the broad range of studies conducted to support a determination of the effectiveness of a new animal drug, certain of the controls listed below would be appropriate and preferred depending on the study conducted:

(i) *Placebo concurrent control.* The new animal drug is compared with an inactive preparation designed to resemble the new animal drug as far as possible.

(ii) *Untreated concurrent control.* The new animal drug is compared with the absence of any treatment. The use of this control may be appropriate when